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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/153,133	09/15/1998	D. DUKE LEE	04712/038002	5068

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EXAMINER	
SOROUSH, LAYLA	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
09/23/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	09/153,133	LEE ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *16 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45,46,58,59,73 and 75-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,46,58,59,73 and 75-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 16, 2009. Claims 45-46, 58-59, 73, and 75-77 are pending.

In view of applicants' amendments to the claims and the presentation of additional claims, the following rejections are made:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45, 46, 58-59, 73 and 75-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reyveld (US Patent 4,016,252), in view of Gerhard et al. (US Patent 5,085,861), and Constantz et al (US Patent 5,782,971).

Relyveld teaches the state of art for using calcium phosphate to improve the efficacy of vaccine formulations. Reyvald teaches injectable gel calcium phosphate vaccine formulations comprising an immunogens from various bacteria (comprise nucleic acid molecules) and viruses (see abstract, col 2, lines 1-5, col 3-4). The calcium

to phosphate ratio in gel formulation of Relyveld is from 1.62 to 1.85 (abstract, col 2 lines 1-15, col 3-4). Reyveld also teaches mixed vaccines by the addition of a calcium phosphate gel which has adsorbed a specific antigen, to a solution containing one or several other antigens. Therefore, Reyveld teaches the appropriate range of calcium and phosphate concentrations in the final formulation. The vaccines are made to treat patients which encompass humans.

Reyvald lacks in teaching a paste formulation having about 40% solid content, an amorphous calcium phosphate or poorly crystalline apatitic calcium phosphate, and the second calcium phosphate.

Gerhard disclose calcium phosphate containing compositions comprising biocompatible calcium phosphate ceramics that can be in the form of an injectable or moldable paste and will solidify within 10 minutes after administration (see abstract; Col 7, lines 30-46, 60-67; Col 8, lines 1-20; examples 2-3). Gerhard's compositions contain active agents that are readily used in treatment of cancers such as bone tumor (Col 13, lines 45-67).

Constantz et al teach amorphous calcium phosphate containing compositions that are used as suitable drug delivery vehicles (Col 2, lines 60-67; Col 6, lines 61-63). Constantz specifically teaches paste formulations of calcium phosphate that are capable of hardening after administration at the site of interest (Col 6, lines 40-64). Constantz's composition comprise about 15 wt% of the dry ingredient (solid component) having particle sizes of about 0.5- 500 microns (Col 5 lines 1-3; and lines 14-25). Constantz further indicates that one of ordinary skill in the art would be able to modify

the viscosity of his composition by varying the percentages of solids in his composition, thus allowing for ease of administration (Col 6, lines 32-39). Constantz suggests the use of an additional calcium phosphate and also states that the calcium to phosphate ratio of such compositions should be about 1.6 to about 1.8 (see Col 3, lines 5-20; Col 5, lines 1-10, claims 1-5). Suitable calcium sources include calcium carbonate, calcium oxide, calcium hydroxide, calcium halide, e.g. calcium fluoride, and the like, as well as calcium phosphates, such as tetracalcium phosphate, tricalcium phosphate, dicalcium phosphate and its dihydrate, monocalcium phosphate and its monohydrate, and the like, where such additional calcium sources may act as bases, acids, sources of counterions and the like, depending on the precise nature of the calcium source.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to modify physical characteristics of Reyveld's composition into an injectable paste, as suggested by Gerhard and Constantz, and formulate a hardenable calcium phosphate formulation that is easily administered to a site of interest. One would be motivated to add the anticancer agent into an injectable paste because the ordinary artisan would have had a reasonable expectation of success in achieving the same results of ease of administration to a site such as a tumor. Finally, absent a showing of unexpected results, to achieve optimal clinical effects, the ordinary artisan would have had reasonable expectation of success to optimize the solid content concentrations of such formulation through the addition of a second calcium phosphate by routine experimentation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 45, 46, 58-59, 73 and 75-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56 and 57 of U.S. Patent No. US 6541037 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the prior art is A vehicle for delivering a biologically active agent comprising: a calcium phosphate source consisting essentially of an amorphous calcium phosphate (ACP) and an acidic calcium phosphate; an aqueous solution in an amount to provide a paste of formable or injectable consistency with the calcium phosphate source, the paste being capable of hardening in association with an endothermic reaction; and a biologically active agent contained in or on the paste whereas the claims herein are a delivery composition comprising: a) calcium phosphate comprising an amorphous calcium phosphate (ACP) or a poorly crystalline apatitic (PCA) calcium phosphate; and b) an antigen or vaccine

wherein said calcium phosphate comprises greater than or equal to 40 wt% of said composition, and wherein said composition is formulated as an injectable paste that hardens in an endothermic reaction.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a vaccine or antigen into the composition. The motivation comes from the teaching that a biologically active agent is delivered using the ACP vehicle. Hence a skilled artisan would have reasonable expectation of success to incorporate the biologically active agents, vaccine or antigens.

Response to Arguments

Applicants argue "Applicants have complied with all of the conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120. Applicants respectfully request acknowledgement that the priority date of the present application is October 16, 1996." It is Examiners contention that there is no support for the limitation "said calcium phosphate comprises greater than or equal to 40 wt% of said composition" in Applic. No. 08/729,342 (October 16, 1996). The priority of October 16, 1996 is not granted.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one would be

motivated to add the anticancer agent into an injectable paste because the artisan would have had reasonable expectation of success in achieving similar ease of administration results to a site such as a tumor.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617